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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1627	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,669	COUTRE, STEVEN	
	Examiner	Art Unit	
	SAMIRA JEAN-LOUIS	1627	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 August 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20-39* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/06/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Arguments

This Office Action is in response to the amendment submitted on 08/06/09. Claims 20-39 are currently pending in the application, with claims 1-19 having being cancelled. Accordingly, claims 20-39 are being examined on the merits herein.

Receipt of the aforementioned amended claims and Information Disclosure Statement (IDS) is acknowledged and has been entered.

Applicant's argument with respect to the rejection of claims 9 and 14-16 under 35 U.S.C. § 112, second paragraph has been fully considered. However, given that claims 9 and 14-16 are now cancelled, such rejection is now moot. Consequently, the rejection of claims 9 and 14-16 under 35 U.S.C. § 112, second paragraph is hereby withdrawn.

Applicant's argument with respect to the rejections of claims 3, 8-9, and 14-16 under 35 U.S.C. § 101 and 112, second paragraph has been fully considered. However, given that claims 3, 8-9, and 14-16 are now cancelled, such rejections are now moot. Consequently, the rejections of claims 3, 8-9, and 14-16 under 35 U.S.C. § 101 and 112, second paragraph are hereby withdrawn.

Applicant's argument with respect to the rejection of claims 3, 8-9, and 13-16 under 35 U.S.C. § 112, first paragraph has been fully considered. However, given that

claims 3, 8-9, and 13-16 are now cancelled, such rejection is now moot. Consequently, the rejection of claims 3, 8-9, and 13-16 under 35 U.S.C. § 112, first paragraph is hereby withdrawn.

Applicant's argument with respect to Longley who merely provides a theoretical basis to experiment with kit inhibitors for the treatment of mastocytosis but is clearly speculative has been fully considered. Applicant further argues that Longley does not provide a reasonable expectation that the experiment would be successful. Such arguments are not persuasive as the Examiner contends that Longley in view of Goekjian does indeed render obvious applicant's invention. Specifically, the Examiner directs applicant's attention to Longley who teaches that studies have shown that mutations affecting the protein coding region of the c-kit proto-oncogene are known to cause some forms of mastocytosis. Additionally, Longley teaches that activating mutations have been found in neoplastic mast cells of patients with mastocytosis thereby implicating c-kit in the causation of the disease. As a result, Longley proposes that inhibition of activating-kit with kit inhibitors should therapeutically be useful in the treatment of mastocytosis. In fact, Longley teaches that studies tested various c-kit (i.e. kit or KIT) inhibitors and found that the various inhibitors were variably effective in inhibiting both wild-type kit and kit with activating mutations (see pg. 691). While the kit-inhibitors were not all potent in their inhibition, all inhibitors exerted some effects on the kit-tyrosine kinase and caused the reduction of the c-kit's phosphorylation. This suggests to one of ordinary skill in the art that kit-inhibitors should help in alleviating the

activation of the c-kit receptor and one of ordinary skill in the art would have indeed expected some successful results since Longley demonstrated some level of inhibition among the various c-kit inhibitors tested.

Given that Longley did not teach midostaurin or PKC412 as the kit-kinase inhibitor in the treatment of mastocytosis, Goekjian was therefore provided to demonstrate why one of ordinary skill in the art would have found it obvious to try and obvious to utilize PKC-412 as the kit-inhibitor in the treatment of mastocytosis as taught by Longley. Goekjian teaches that midostaurin or PKC412 is a first generation staurosporine analog that has been found to inhibit c-kit. Particularly, PCK412 or midostaurin was found to achieve greater level of kinase selectivity (i.e. c-kit selectivity) and potential therapeutic index and tended to be non-toxic. Consequently, the Examiner contends that one of ordinary skill in the art would have found it obvious to try PKC412 as the c-kit inhibitor in the treatment of mastocytosis since Longley teaches that c-kit inhibitors can be effectively used to treat mastocytosis and is expected to work to a certain degree and in view of Goekjian who teaches PKC412 as a selective c-kit inhibitor known to be therapeutically effective and non-toxic. In light of such disclosures, the Examiner maintains that Longley in view of Goekjian does indeed render obvious applicant's invention. However, in light of applicant's amendment and cancellation of claims 1-19, the rejection is hereby withdrawn.

Regarding applicant's arguments that Longley teaches kit inhibitors with variable activity against the activating mutations and that such disclosure merely lead a skilled

artisan to try to find kit inhibitors that target the appropriate activated mutant kit, such arguments are not found persuasive as Longley did show that the kit inhibitors worked in inhibiting c-kit activity to a certain extent. While the c-kit inhibitors were not all potent in their inhibition, the experiments (see Longley, pgs. 691-692) were effective in attenuating the phosphorylation of c-kit to a certain degree. Thus, such results would have motivated one of ordinary skill in the art to try PKC412 for inhibiting c-kit and for subsequent treatment of mastocytosis since Longley teaches c-kit inhibitors for such treatment and in light of the disclosure of Goekjian who teaches that PKC412 is a selective inhibitor and has low toxicity.

As for applicant's arguments that Longley demonstrated variable activity against the mutant c-kit involved in mastocytosis and thus does not provide a general teaching that kit kinase inhibitors can effectively kill mast cells, such arguments are again not found persuasive as Applicant is equating variable effect as no effect. While the inhibitors did not result in 100% inhibition of cell growth or 100% dephosphorylation (i.e. reduction of kinase activity), all of the inhibitors demonstrated inhibition of c-kit activity (i.e. via reduction of phosphorylation) and subsequent reduction in cell numbers (i.e. low cell growth). Such results would have indeed prompted one of ordinary skill in the art to try PKC412 in the treatment of mastocytosis and one of ordinary skill in the art would have had a reasonable expectation of success as Longley demonstrated an effect, though variable, of such inhibitors on c-kit.

Applicant's argument that Goekjian does not teach the ability of PKC412 to inhibit kit with the D816V mutation has been fully considered. Applicant further argues that because Goekjian does not provide any basis for the skilled artisan to expect PKC412 to have activity against any particular activated mutant kit or more particularly the activated mutant kit associated with mastocytosis, and thus the combined disclosure of the references would not lead the skilled artisan to have any expectation with respect to PKC412's potential for treating mastocytosis. Such arguments are not persuasive as the Examiner contends that such disclosure is not required in order for one of ordinary skill in the art to try PKC 412 in the treatment of mastocytosis. Given that Longley teaches and suggests that c-kit inhibitors are therapeutically effective in treating mastocytosis and given that Goekjian teach PKC412 as a selective c-kit inhibitor with low toxicity, the Examiner maintains that one of ordinary skill in the art would have found it obvious to try and be motivated to utilize PKC412 with a reasonable expectation of success since Longley demonstrated that the c-kit inhibitors were all effective to some degree in inhibiting wild-type c-kit and mutant c-kit (i.e. the equivalent of the human D816V mutation). As a result, the Examiner maintains that in view of the teachings of Longley and Goekjian, one of ordinary skill in the art would have had a reasonable expectation that PKC412 would be effective to a certain degree. However in view of applicant's amendment and cancellation of claims 1-19, the rejection is hereby withdrawn.

As for applicant's arguments that the prior art teaches that PKC412 is much more potent against the c-kit mutation D816V, such arguments are not found persuasive as applicant's arguments do not commensurate in scope with the claims. Nowhere in the instant claims is a recitation delineating any potency of PKC412. The claims as presently recited are directed to a treatment of mastocytosis utilizing PKC412. Longley suggests the use of c-kit inhibitors and demonstrated various c-kit inhibitors who were effective in inhibiting c-kit activation to various degrees and that c-kit is involved in the causation of the disease mastocytosis. Goekjian teaches the use of PKC412 as a selective c-kit inhibitor and a c-kit inhibitor with low toxicity. Consequently, in view of the aforementioned teachings, the Examiner contends that regardless if Goekjian teaches that PKC412 is effective against mutant c-kit, one of ordinary skill in the art would have indeed been motivated to try PKC412 and would have had a reasonable expectation of success since Longley demonstrated that various c-kit inhibitors were effective in inhibiting to various degrees the kinase, c-kit wild type and mutants. As a result, the Examiner maintains that the 103(a) rejection over Longley in view of Goekjian was indeed proper. However in view of applicant's amendment and cancellation of claims 1-19, the rejection is hereby withdrawn.

As for Ma, such reference was provided to demonstrate that mastocytosis is known in the art to be resistant to imatinib (i.e. STI571). Given that Goekjian teaches that PKC412 is a potent inhibitor of c-kit and has low toxicity, the Examiner contends that one of ordinary skill in the art would have found it obvious to try and utilize PKC412

in mastocytosis resistant to imatinib with a reasonable expectation of success in light of Longley who demonstrated that various c-kit inhibitors inhibited c-kit to a certain level. As a result, Longley in view of Goekjian and in further view of Ma does indeed render obvious applicant's invention. Caravatti, on the other hand, was provided to demonstrate appropriate dosages and mode of administration to use for the c-kit inhibitor, PKC412, as taught by the prior art. Thus, the Examiner maintains that it would have been obvious to one of ordinary skill in the art to utilize PKC412 in such dosages since Caravatti teaches that dosages can be varied depending on the disease to be treated, the patient and severity of the condition.

For the foregoing reasons, the rejections of record are withdrawn. However in view of applicant's amendment, the following objection, 112, first paragraph and modified 103 (a) Final rejections are being made.

Specification

The disclosure is objected to because of the following informalities: specification is missing. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

> art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27 and 37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

As stated by the court in Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886, 1892 (CAFC 2004), regarding the written description requirement:

> The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described.

In this instant application, applicant did not adequately describe a method of treatment wherein up to 150 mg per day of midostaurin or PKC412 is administered as delineated in the claim(s) (i.e. claims 27 and 37). While applicant described administration of the aforementioned compound in an amount between 100-300 mg or between 125-250 mg, nowhere did applicant describe administration up to 150 mg of the aforementioned compound thus rendering it impossible for one skill in the art to envisage the exact ranges encompassed by the invention. Consequently, due to this lack of written description, the Examiner contends that applicant does not possess support for such recitation and that the specification (i.e. PgPub in this case) did not reasonably convey to those skilled in the art that the applicant was in possession of such limitation as of the date of invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 20 is rejected under 35 U.S.C. 103 (a) as being unpatentable over Longley et al. (Hematology/Oncology Clinics of North America,, Vol. 14, No. 3, pgs. 689-695, previously cited) in view of Goekjian et al. (Experts Opinions on Investigational Drugs, December 2001, Vol. 10, No. 12, pgs. 2117-2140, previously submitted).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Longley et al. teach that the treatment of mastocytosis is designed to prevent or ameliorate the deleterious effects of mast cell mediators rather than to eliminate the mast cells which produce and release them (see pg. 689). Longley et al. further teach that current forms of therapy while they lead to a decrease of mast cell numbers also cause significant adverse side effects (see pg. 690, paragraph 2). However, recent studies have suggested that mutations affecting the protein coding region of the c-kit proto-oncogene may cause some forms of mastocytosis (see pg. 690, paragraph 3). Specifically, Longley teaches that one group consists of mutations in codon 816 of human c-kit or its equivalent positions in other species, resulting in single residue substitution for Asp816 in the activation loop of the receptor kinase domain (pg. 691). C-kit encodes a receptor tyrosine kinase whose cognate ligand is mast cell growth factor. Activation of mast cell growth factor receptor or kit stimulates mast cell growth and prevents apoptosis. Furthermore, activating mutations have been found as somatic mutations in the neoplastic mast cells of patients with mastocytosis. Thus, the consistent finding of activating c-kit mutations in mast cell tumors, together with the ability of activated kit to stimulate mast cell proliferation and transformation, suggests that these mutations are necessary if not sufficient, for some forms of mastocytosis (see pg. 690, last paragraph). Moreover, Longley et al. teach that inhibiting activating kit with kit inhibitors might be therapeutically useful in mastocytosis, might provide symptoms relief, decrease mast cell load and might eventually provide a cure by completely eliminating the neoplastic mast cell clone (see pg. 690, last paragraph). Additionally,

Longley et al. demonstrated that kit kinase inhibitors can effectively kill neoplastic mast cells which cause some forms of mastocytosis by using various kit inhibitors and demonstrating their various levels of inhibition in both wild type kit and p815 mutant cells (i.e. cells possessing mutation equivalent to D816V; see pg. 693, last paragraph and figs. 1-2).

Longley et al. do not specifically teach midostaurin or PKC412 as the kit kinase inhibitor effective in treating mastocytosis.

Goekjian et al. teach midostaurin or PKC-412 as an inhibitor of PKC that effectively inhibit signal transduction pathways (see pg. 2117, abstract). Goekjian et al. also teach that first generation staurosporine analogues CGP41251 or PKC-412 or midostaurin achieves a greater level of kinase selectivity and potential therapeutic index as a PKC inhibitor and tends to be non-toxic in light of mixed kinase inhibition that it exhibits (see pg. 2123. right col., last paragraph). Importantly, Goekjian et al. teach that midostaurin is a broad range kinase inhibitor and has been found to inhibit the stem cell factor receptor c-kit at approximately micromolar concentration (i.e. midostaurin is a kit inhibitor; see pg. 2124, table 1 and Section 3.1).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to utilize the midostaurin of Goekjian et al. for the treatment of mastocytosis since Goekjian et al. teach midostaurin as a non-toxic kit inhibitor and

Longley et al. teach that mastocytosis can be best treated with kit inhibitors. Thus, given the teachings of Longley and Goekjian, one of ordinary skill would have been motivated to try and motivated to utilize midostaurin in light of the disclosures of Goekjian and Longley with the reasonable expectation of providing a method effective in treating mastocytosis with a low toxicity staurosporine derivative.

Claims 30 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Longley et al. (Hematology/Oncology Clinics of North America,, Vol. 14, No. 3, pgs. 689-695, previously cited) in view of Goekjian et al. (Experts Opinions on Investigational Drugs, December 2001, Vol. 10, No. 12, pgs. 2117-2140, previously submitted) as applied to claim 20 above and in further view of Ma et al. (Blood, 2002, Vol. 99, No. 5, pgs. 1741-1744, previously cited).

The Goekjian and Longley references are as discussed above and incorporated by reference herein. However, Goekjian and Longley do not teach treatment of mastocytosis resistant to imatinib.

Ma et al., however, teach that adult-type or sporadic adult-type human mastocytosis (SAHM) is characterized by mutations in c-kit codon 816, which causes constitutive activation of the KIT kinase (i.e. D186v mutant kit or c-kit; see pg. 1741, left col. paragraph 1). Ma et al. also teach that mast cell lines and canine mast cell tumors also express activating c-kit mutations and small molecules that inhibit mutant activated

KIT was able to effectively kill these cell lines (see pg. 1741, left col., paragraph 1). Ma et al. further teach that STI571 (i.e. imatinib) while effectively in inhibiting regulatory mutations or RT mutations did not significantly inhibit enzymatic site or EST mutations associated with SAHM (see abstract, pg. 1741). Importantly, Ma et al. demonstrated that mast cell lines with EST mutations was not inhibited by STI571 suggesting that the kit inhibitor STI571 is effective against certain mastocytosis and not SAHM (see abstract pg. 1741). This suggests that certain mastocytosis is resistant to imatinib.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to try the midostaurin of Longley in sporadic adult-type mastocytosis since Goekjian teaches that midostaurin is a potent inhibitor of c-kit with low toxicity properties. Given the teachings of Longley, Goekjian, and Ma, one of ordinary skill would have been motivated to try midostaurin in light of the disclosures of Goekjian, Longley, and Ma with the reasonable expectation of providing a method effective in treating sporadic adult type mastocytosis and imatinib-resistant mastocytosis with a potent and low toxicity staurosporine derivative.

Claims 21-28, 31-33, and 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Longley et al. (Hematology/Oncology Clinics of North America,, Vol. 14, No. 3, pgs. 689-695, previously cited) in view of Goekjian et al. (Experts Opinions on Investigational Drugs, December 2001, Vol. 10, No. 12, pgs. 2117-2140, previously submitted) as applied to claim 20 above and in further view

of Ma et al. (Blood, 2002, Vol. 99, No. 5, pgs. 1741-1744, previously cited) as applied to claims 30 and 34 and in further view of Caravatti et al. (U.S. 5,093,330, previously cited).

The Goekjian and Longley references are as discussed above and incorporated by reference herein. However, Goekjian and Longley do not teach the forms of the composition, the exact dosage of midostaurin to be used in the treatment of mastocytosis or the mode of administration.

Caravatti et al. teach N-substituted derivatives of staurosporine including N-benzoyl-staurosporine (see abstract and col. 28, lines 45-57). Specifically, Caravatti teaches that the pharmaceutical compositions containing the aforementioned active ingredients can be administered enterally, perorally (i.e. orally), or rectally wherein the peroral administration is in an amount of 5-500 mg (see col. 23, lines 21-29). Caravatti et al. further teach that the aforementioned active ingredients can be administered in an effective amount in a daily dosage from 1 to 1000 mg depending on the species, body weight, age, individual conditions, desired method of administration and the type of disease (see col. 23, lines 3-29). Additionally, Caravatti et al. teach that the composition can be formulated as soft sealed capsules containing gelatin and plasticizers (i.e. soft gel; instant claims; see col. 23, lines 57-68 and col. 24, lines 1-11). Caravatti et al. further teach that the aforementioned pharmaceutical preparations can be formulated in a manner known per se (col. 24, lines 22-25). As for the mode of

administration, the Examiner contends that it would be well within the purview of the skilled artisan to administer midostaurin at least daily for at least one week, discontinue the treatment if patient improves, and subsequently restarting treatment as desired during the course of experimentation depending on the desired treatment as taught by Caravatti et al.

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to vary the mode of administration and treat mastocytosis in the range of 1 to 1000 mg or 5-500 mg for peroral administration since Caravatti et al. teach that one of ordinary skill in the art can vary the concentration depending on the desired mode of administration, disease, and the patient to be treated. Thus, given the teachings of Goekjian, Longley, Ma and Caravatti et al., one of ordinary skill would have been motivated to utilize midostaurin and vary the dosages and mode of administration in light of the disclosures of Goekjian, Longley, Ma and Caravatti with the reasonable expectation of providing a method effective in treating mastocytosis with a potent and low toxicity staurosporine derivative.

Claims 29 and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Longley et al. (Hematology/Oncology Clinics of North America,, Vol. 14, No. 3, pgs. 689-695, previously cited) in view of Goekjian et al. (Experts Opinions on Investigational Drugs, December 2001, Vol. 10, No. 12, pgs. 2117-2140, previously submitted) as applied to claim 20 above and in further view of Ma et al. (Blood,

2002, Vol. 99, No. 5, pgs. 1741-1744, previously cited) as applied to claims 30 and 34 and in further view of Caravatti et al. (U.S. 5,093,330, previously cited) as applied to claims 21-28, 31-33, and 35-38 in further view of Matthews et al. (U.S. 2002/0061873).

The Longley, Goekjian, Ma, and Caravatti references are as discussed above and incorporated by reference herein. However, Longley, Goekjian, Ma, and Caravatti do not teach the composition as a microemulsion.

Matthews et al. teach N-benzoyl staurosporine (i.e. midostaurin or PKC 412) compositions with high bioavailability (see abstract). Matthews et al. further teach that the pharmaceutical formulations produce aqueous microemulsions which are stable for up to one day or longer (see pg. 5, paragraph 0067).

Thus, to one of ordinary skill in the art at the time of the invention would have found it obvious to formulate the composition as a microemulsion since Matthews et al. teach that midostaurin can be made as aqueous microemulsions that are stable for up to one day or longer. Thus, given the teachings of The Longley, Goekjian, Ma, and Caravatti et al., one of ordinary skill would have been motivated to formulate midostaurin as a microemulsion with the reasonable expectation of providing a method effective in treating mastocytosis with a potent, stable and low toxicity staurosporine derivative.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samira Jean-Louis whose telephone number is 571-270-3503. The examiner can normally be reached on 7:30-6 PM EST M-Th. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/S. J. L. /

Examiner, Art Unit 1627

12/10/2009

/SREENI PADMANABHAN/

Supervisory Patent Examiner, Art Unit 1627